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Original article

Endoscopic endonasal trans-sphenoidal approach for pituitary fossa tumor: Outcome analysis of 39 consecutive procedures

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ABSTRACT

Background: To assess postoperative rhinological complaints, length of hospital stay and complications related to endoscopic, endonasal trans-sphenoidal procedures.
Patients and methods: From May 2001 through May 2007, a retrospective analysis was conducted on a series of 39 patients that underwent endonasal surgery and 9 patients that had craniotomy removal of pituitary tumors. Questionnaires were filled out at both 2 weeks and 3 months after surgery, most of which were completed in the outpatient department if the patient was discharged. Nasal packing lasted for 72 h in 29 patients, but not in the last 10 patients.
Results: Of the 12 patients with preoperative headache, 50% had complete resolution, 33% had partial resolution and 17% reported no change. The frequency of rhinological complaints declined between the two questionnaires ($p < .001$). After 3 months, 64–84% of patients had no rhinological complaints, while 2.5% had severe complaints. Of the 9 patients with complications, rhinological complaint severity was similar to those without complications ($p < .001$).
Conclusions: The direct endonasal trans-sphenoidal approach for pituitary fossa tumor is associated with a rapid rhinological recovery, shorter hospital stay and a low occurrence of serious long-term sinonasal complaints.

1. Introduction

The first transcranial operation on a pituitary adenoma was performed by Victor Horsley in 1904; 3 years later, the first trans-sphenoidal operation was performed by Hermann Schloffer.[1,2] A direct endonasal approach to the sella, requiring removal of the middle turbinate and part of the nasal septum, was first described by Hirsch in 1910.[1,2] In 1912, Cushing introduced the sublabial trans-sphenoidal approach, which Dott, Guiot,[3] and Hardy[4,5] repopularized in the 1950s and 60s.[1,2] Although the sublabial approach has been the favored surgical route to the sella for many years, an endonasal approach with the operating microscope, and more recently with the endoscope alone or an endoscope-assisted approach, has gained popularity, both for neurosurgeons and their patients.[6–10]

The endonasal approach, currently used by many pituitary surgeons, was first described by Griffith in 1987 as a refinement of Hirsch's original approach.[11] Instead of three mucosal tunnels, as in the sublabial route, or one mucosal tunnel, as utilized in the transseptal approach, the direct endonasal approach requires no mucosal tunnels and only one mucosal incision in the posterior nasal cavity[12] (Fig. 1) (Fig. 2). We have been using the direct endonasal approach for all pituitary tumors for many years. This report documents our experiences with 39 patients who underwent endonasal resection of a pituitary adenoma or other sellar lesions and 9 patients who received craniotomy removal of a pituitary tumor.

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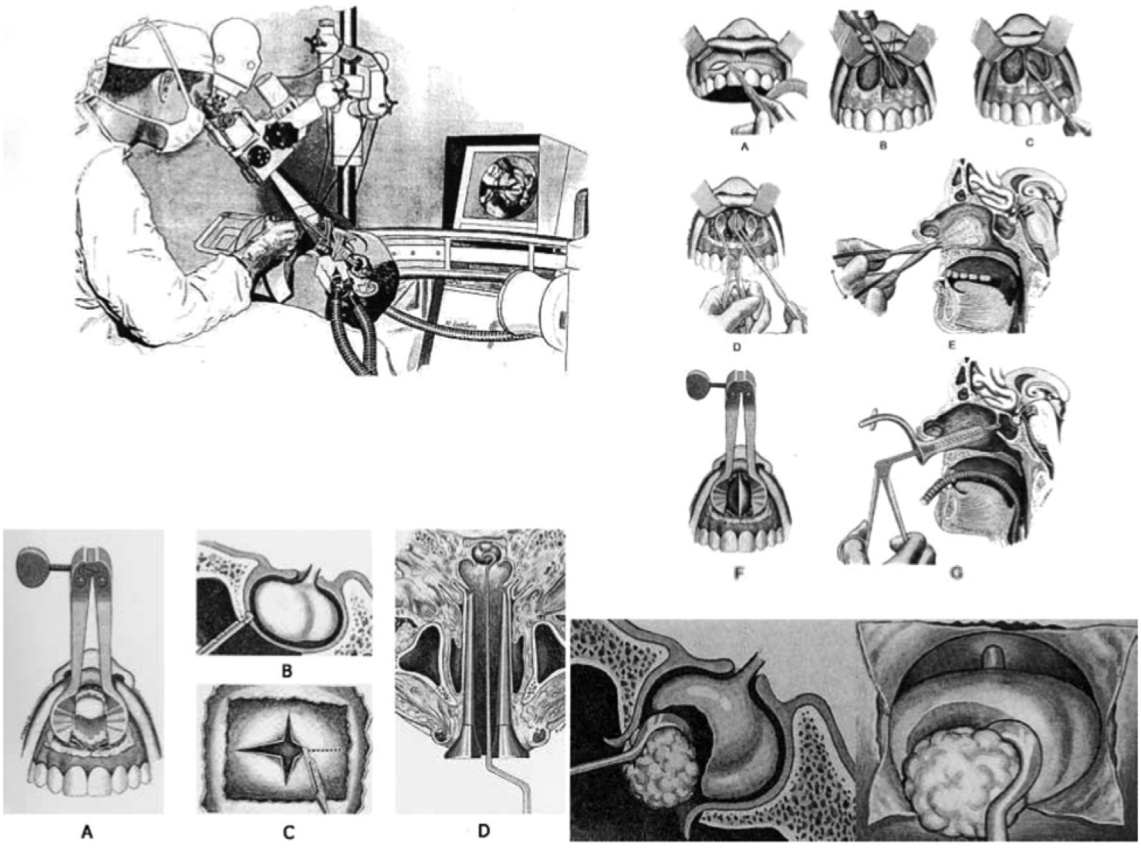

Fig. 1. Right: Illustrations showing Hardy's sublabial trans-septal trans-sphenoidal approach. A: Sublabial incision. B: Elevation of nasal mucosa from the floor. C: Submucosal dissection from the septum. D: Resection of the cartilaginous septum with a swiveled knife. E: Sagittal view of the submucosal dissection. F: Introduction of the self-retaining speculum that reveals the vomer, which resembles the keel of a ship. G: Sagittal view of the speculum in position. Upper Right: Operative drawing showing the sella turcica portion of the procedure. A: Resection of the vomer and the floor of the sphenoid sinus, exposing the sella turcica. B: Opening of the sellar floor with a rongeur. C: Cruciate incision made in the dura of the sella turcica. D: Horizontal view of the strict midline approach to the sella turcica. Lower Right: Drawing showing selective removal of a pituitary microadenoma while preserving pituitary function. (Reprinted with permission from Hardy J: J Neurosurg 34:582–594, 1971.)

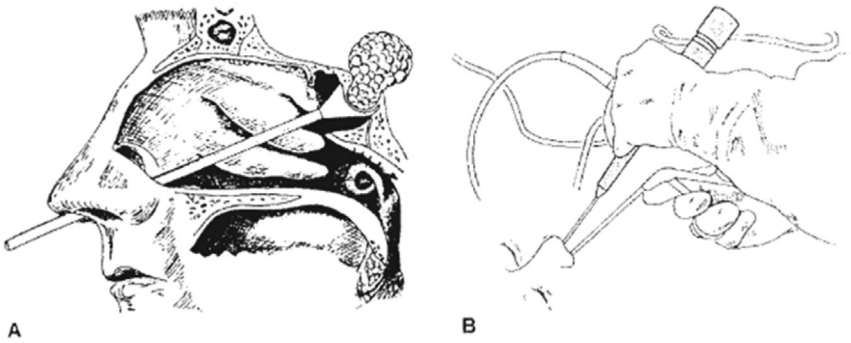

Fig. 2. Drawings showing an endonasal endoscopic approach to the sella turcica. A: Note the absence of septal or alar incisions. B: The endoscope is held in the surgeon's nondominant hand and instruments are held in the dominant hand until the anterior sphenoidotomy is made. (Reprinted from Surg Neurol 47, Jho HD, et al: Endoscopic pituitary surgery: an early experience, 1997, with permission from Elsevier Science.).

2. Methods

2.1. Patient population

Thirty-nine patients who underwent endonasal surgery for a pituitary adenoma or other parasellar tumors and 9 patients who received craniotomy removal of a pituitary tumor, at the Department of Neurosurgery, Mackay Memorial Hospital, between May 2001 and May 2007, were eligible for this study. Patient charts were reviewed for demographics, length of stay and surgical complications.

2.2. Questionnaire

Questionnaires were filled out at 2 weeks and 3 months after surgery; most were filled out in the outpatient department, if the patient was discharged. Patients were asked questions related to headaches and to 4 areas related to rhinological recovery,

including nasal congestion, decreased nasal airflow and decreased olfaction.

2.3. Surgical technique

We performed endonasal surgery as it was originally described by Griffith and Veerapen,[11] with several modifications described in this section. Following general anesthesia, patients were placed in the supine, semi-slouch position, with the head resting freely on the bed and angled approximately 30° toward the left shoulder, as described by Laws.[13] A few key points regarding rhinological aspects of the approach warrant emphasis. First, initial preparation of each nasal cavity involved only a brief swabbing with betadine-soaked, cotton-tipped applicators; and injection of vasoconstrictors. Second, during the initial approach, care was taken to minimize mucosal trauma and bleeding from the hand-held speculum and insertion of the modified Hardy speculum. Third, the only mucosal incision deliberately made was at the junction of the posterior nasal septum and sphenoid keel. Fourth, entering the sphenoid sinus, the only mucosa typically removed was that lining the anterior sphenoid sinus wall and overlying the sella. Fifth, upon procedure completion, after removing the modified Hardy speculum, the hand-held speculum was again used to explore both the operated and nonoperated nasal cavities to identify significant mucosal bleeding, which was stopped with the bipolar, Gelfoam or Surgifoam. Sixth, the middle turbinate on the side of the approach, which was out-fractured by the speculum at the start of the procedure, was repositioned by medializing it toward the nasal septum.

Twenty-nine (74%) patients had abdominal fat grafts and nasal packing placed for 72 h to prevent CSF leak and prevent hemorrhage. In the subsequent 10 patients, nasal packing and abdominal fat graft were not used. During the first postoperative night, patients were given a humidified face tent and decongestants were available upon request. Antibiotics were given for a period of 72 h after surgery.

Analysis included demographics, length of stay, complication rates, rhinological complaints, preoperative headaches, visual functioning and endocrinological outcomes with any noted complications. We also included subgroup analyses of patients with nasal packing as compared to its absence, complications as compared to their absence and comparison of craniotomy approaches.

2.4. Statistical analysis

Numerical data (e.g. hospital duration) were analyzed through ANOVA. Differences between groups (craniotomy vs endonasal techniques, etc.) were tested by Chi-squared and Fisher's exact test.

3. Results

3.1. Demographics

In this study, the 39 endonasal trans-sphenoidal patients ranged in ages from 21 to 72 years, and 23 (59%) were female. Furthermore, pathology included 37 (94%) pituitary adenomas and 2 (5%) Rathke's cleft cysts (Table 1).

3.2. Length of stay and complication rate

The median length of stay was 12 days (range: 4–48), with more than 48% of patients going home by day 7 (Fig. 3). Nine (23%) patients had surgical complications, the most common of which were anterior hypopituitarism of one or more hormonal axis (7%), postoperative CSF leak (5%) and persistent diabetes insipidus (2%). In addition, there was 1 patient with transient postoperative meningitis. In the entire cohort, there was 1 carotid artery injury (without neurological sequela) and non-postoperative sellar hematoma. There were no permanent ocular palsies or visual worsening. However, there was one mortality. Of the 39 patients, 30 had non-surgical complications (Table 2).

Table 1
Pathological diagnoses in 39 patients.

Pathology	No. of patients
Pituitary adenoma	37
Endocrine-inactive	22
Prolactinoma	7
Cushing's disease	4
Acromegaly	4
TSH secreting	0
Rathke's cleft cyst	2
Total	39

3.3. Questionnaire results

Postoperative complaint frequency, including headache, nasal congestion, decreased airflow and decreased olfaction, declined significantly in the period between the two questionnaires ($p < .001$) (Fig. 4).

3.4. Preoperative headache

Of the 12 patients with preoperative headaches, 6 had complete resolution, 3 had partial resolution and 3 reported no change.

3.5. Visual function and other cranial nerve palsies

Of the 22 patients with preoperative visual defects, 16 (72%) had improved vision and 6 (27%) had no change. No patients experienced postoperative worsening of visual acuity or visual fields, or new cranial nerve palsies.

3.6. Endocrinological outcomes

Four patients (10%) had endocrinological complications, all of whom had harbored macroadenomas. Three patients lost anterior pituitary functioning of the thyroid axis and required long-term thyroxin support. One patient developed permanent diabetes insipidus (DI) and required long-term Desmopressin (minirin 0.1 mg twice daily) (Table 3). Transient DI was observed in 10% of patients and it typically resolved within 3 days of surgery. Transient delayed hyponatremia was observed in 1 patient.

3.7. Surgical and medical complications

There was one mortality, a 46-year-old patient with an endocrine-inactive macroadenoma and a history of arrhythmia and atrial fibrillation. He suffered from post-operative DI. Fluid support, desmopressin and vasopressin were used. However, sudden cardiac arrest occurred the night following the operation, which cardiopulmonary resuscitation failed to prevent.

There was one major surgical complication, a carotid injury. This occurred in a 56-year-old man with a 2-cm-wide GH-secreting adenoma. He suffered an inadvertent puncture injury to the left internal carotid artery, which was packed with Gelfoam and fat graft. Twenty days after surgery, there was right eye pain and swelling. A carotid-cavernous fistula was identified on follow-up

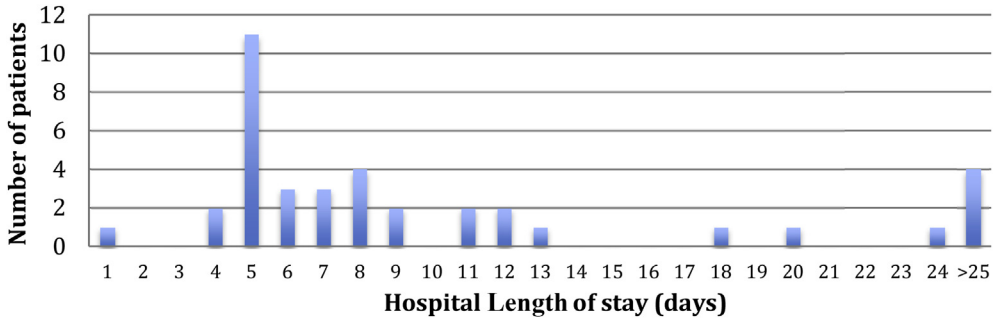

Fig. 3. Hospital stay for all 39 patients. Overall, 48% of patients were discharged by postoperative day 7.

Table 2
Complications of endonasal trans-sphenoidal surgery.

Complication	No. of patients
Persistent DI	1
CSF leak	2
Loss of anterior pituitary axis	3
Meningitis	1
Carotid injury	1
Death	1
None	30 (77%)

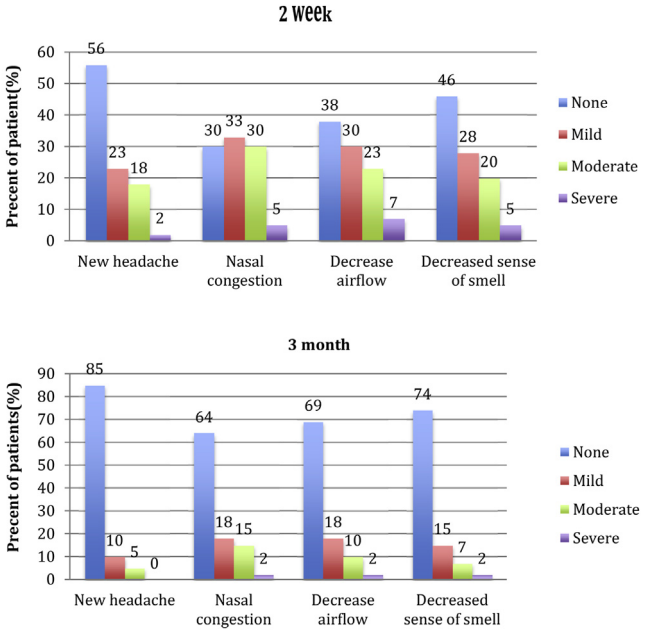

Fig. 4. Postoperative headache, nasal congestion, decreased airflow and decreased olfaction, declined significantly from 2 weeks after surgery to 3 months+ ($p < .001$).

Table 3
Endocrinological outcomes: hormonal losses.

Change in hormonal axis	No. of patients
Anterior gland	
Lost thyroid axis	3
Lost cortisol axis	0
Lost GH axis	0
Posterior gland	
Permanent DI	1
No change in axes	35

angiograms, which was treated on postoperative day 26 through endovascular placement of Guglielmi coils. The patient recovered without any detectable visual deficits.

Postoperative CSF leak occurred in 2 patients; both had intra-operative abdominal fat graft impact. Lumbar CSF drainage was used, after which both patients also suffered from meningitis, which resolved completely in response to a 6-week course of antibiotics. There was no post-lumbar drainage at 7 and 10 days. Both patients made a full recovery, without sequelae.

4. Subgroup analyses

4.1. Nasal packing VS no nasal packing

Regarding the in-hospital postoperative period, more than 82% of patients with packing complained about the packing and/or mouth breathing. At 2 weeks after surgery, patients with packing complained of nasal congestion and decreased nasal airflow (75% and 68%), compared with 3 months after surgery (37% and 30%) and also compared with those without packing (31% and 20%). By 3 months, this difference was lost (p-values all >.1).

4.2. Comparison with craniotomy

Nine patients were in the craniotomy group (Table 4). In this group, the pituitary tumor size for all patients was large, at 3 cm in diameter, and presented a difficult approach using the trans-sphenoidal method. Seven patients had pituitary macroadenoma, one patient had pituitary metastatic neuroblastoma and one had pituitary malignant lymphoma. The craniotomy group median hospital stay was 36.6 days, as compared to 12 days for the endonasal group. The craniotomy group had high rates of new post-operative headaches (44%) and post-operative pneumonia (44%), as opposed to 15 and 0% in the endonasal group ($p < .001$ for all).

Table 4
Pituitary tumor in craniotomy group 9 patients.

Age	F/M	Pathological
32	M	Pituitary macroadenoma
56	M	Pituitary macroadenoma
11	M	Metastatic neuroblastoma
34	M	Pituitary macroadenoma
68	F	Pituitary macroadenoma
65	M	Pituitary malignant lymphoma
67	F	Pituitary macroadenoma
65	F	Pituitary macroadenoma
72	M	Pituitary macroadenoma

4.3. Patients with complications vs. those without

Median hospital length of stay for 9 patients who had surgical or other postoperative complication was 22.9 days (range, 6–48 days) compared to the "without complication" group median hospital length of stay of 6.7 days (range, 4–12 days). Postoperative headache and rhinological complaints at 3 months, rates of new headache (22%), nasal congestion (33%) and nasal airflow decrease (33%) were similar to patients without complications; however, more patients complained of decreased olfaction (55%) ($p < .001$).

Differential diagnosis of malignant diseases arising within the clivus of the adjacent structures of the pituitary fossa.

The main important malignant diseases of the clivus were chordoma, chondrosarcoma, fibrous dysplasia, myeloma, and metastasis arising within the clivus. In clinical presentations of the clivus tumor, patients were noted to be often with cranial nerve palsies or headache.[14,15] Diplopia results from involvement of the abducens nerve in Dorello's canal on the posterior surface of the clivus.[15,16] Endocrinopathy may occur depending on infiltration of the pituitary.

4.4. Chordoma

Chordoma is typically a slow-growing and histologically low grade neoplasm, which is locally invasive and has a high recurrence rate, with a clinical progression similar to malignant tumors. The average 5-year progression-free survival and overall survival are 51% and 78%, respectively.[17]

4.5. Chondrosarcomas

Chondrosarcomas account for 6% of skull-base tumors.[18] They develop from primitive mesenchymal cells[19] in synchondroses of the skull base with a high predilection for the petroclival synchondrosis[20]; therefore, they develop in a paramedian location.[18] Differentiating chondrosarcomas from chordomas is important as the 5-year progression-free survival is >90% for chondrosarcoma compared to around 51% for chordoma.[21]

4.6. Metastasis

Metastasis appears to be less likely than chordoma or chondrosarcoma.[16] The most common primary sites for metastasis were prostate, thyroid, and hepatocellular carcinomas, with the prostatic origin conferring a male predominance.[16] Patients with metastases had a poor prognosis of approximately 10 months survival.[16]

4.7. Plasmacytomas/myeloma

Extramedullary plasmacytomas, bone plasmacytomas and multiple myeloma are monoclonal plasma cell proliferations. Multiple myeloma is considered to be the malignant diffuse final stage.[22]

5. Discussion

This study demonstrates that the standard direct endonasal approach is well tolerated, with relatively few long-term rhinological complaints. The elimination of nasal packing is associated with more nasal congestion and decreased airflow at 2 weeks after surgery. By 3 months after surgery, 64–74% of all patients in the cohort had no rhinological complaints and only 2% had severe rhinological complaints. Persistent nasal congestion, either moderate (15%) or severe (2%), was the most common long-term complaint.

In this study, 12 patients had preoperative headaches, 50% of whom had complete resolution within 2 weeks after surgery. Twenty-two patients had preoperative visual defects, although 16 (72%) of them improved. None of the 39 patients experienced postoperative worsening of visual acuity or visual fields, or new cranial nerve palsies.

Subgroup analysis revealed several findings. Craniotomy patients had longer hospital stays (36 days) and had higher rates of new postoperative headaches and pneumonia (44% each). Finally, in patients with complications in the endonasal group with long term of hospital stay 22 days but headache and rhinological complaints at 3 months, follow-up were similar to patients without complication.

5.1. Rhinological complications and complaints

The endonasal route is perhaps most notable for its minimization of nasal and sinus complications. There were no nasoseptal perforations, hematomas or abscesses seen in this series. In contrast, after sublabial transseptal transsphenoidal surgery, rhinological complications have been known to range as high as 28–35%.[23–25] Eisele et al,[23] reported nasoseptal perforations in 1–13% of patients, upper lip paresthesia in 5–28% of patients,[23] and postoperative anosmia in 5.5% of patients.[24,26] The transseptal endonasal approach, which requires extensive anterior nasal septal dissection, was reported by Sharma[24] to have a relatively high rate of complaints and nasal complications (21%), including septal perforations (7%), synechiae (12%), and a septal abscess (1%), which were in line with Eisele.[23] In another report by Spencer[27] in which the sublabial approach was compared with the trans-septal endonasal approach, postoperative complaints of pain and numbness were noted by 50 and 50% of patients, respectively, after the sublabial approach, and by 25 and 75% of trans-septal patients overall.

5.2. Neurosurgical morbidity rates and hormonal loss

The rates of surgical complications in this series are similar to those reported for several recent trans-sphenoidal series.[12,23,26,28–30] Preservation of anterior pituitary functioning was achieved in most patients, with hormonal loss occurring in only 10% of patients. The rate of permanent DI for patients with adenomas (2%) was similar to previous reports, in which rates generally range from 2 to 5%.[26,29,31,32]

5.3. Carotid artery injury

Although they were thought to occur infrequently (<0.2% in large series involving experienced pituitary surgeons[12,33,34]), the national survey on complications of transsphenoidal surgery, including 958 pituitary surgeons, reported an ICA injury rate of 1.1%.[26] Vascular injury is a major contributor to the mortality associated with the procedure.[26] Cappabianca et al,[35] reported one ICA injury out of 233 trans-sphenoidal endoscopic procedures, which was managed successfully by endovascular treatment. In our study, one patient (2.5%) with a carotid artery injury was managed by endovascular placement of Guglielmi coils and recovered without complications.

5.4. Study limitations

There were two major limitations to this study. First, because routine postoperative rhinological inspections were not performed, it is possible that nasal-septal perforations, synechiae or other sinonasal trauma were not discovered. In particular, such findings may have been presented to those patients who complained of

persistent facial pain, nasal congestion, decreased airflow or decreased sense of smell.

Second, although the questionnaire items were internally consistent and met criteria for good testing, based on the quality control fit statistics provided by the Rasch model, the questionnaire was retrospective with respect to patient impressions, 2 weeks after surgery. Although this raises the question of possible "softening" of one's impressions of the early postoperative surgical experience, there was an almost unanimous decrease in the severity of complaints from the 2-week to the 3-month time point after surgery.

6. Conclusions

The direct endonasal transsphenoidal approach with an operating microscope is associated with a rapid rhinological recovery and a low occurrence of serious, long-term sinonasal complaints. Because it obviates the oral incision, extensive mucosal dissection and nasal packing required of the sublabial transsphenoidal approach, it appears to afford a rhinologically superior patient recovery with fewer sinonasal complaints and a shorter hospital stay. However, not surprisingly, in a small minority of patients, significant discomfort persists after the direct endonasal approach. Whether or not a purely endoscopic endonasal approach can eliminate such complaints remains to be proven.

Conflict of interest

None.

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